

REMARKS

1. Election/Restriction

1.1. We previously requested rejoinder of groups VII (claims 43, 88 and 90) and IX (claims 43, 44, 88) with elected group VIII (claims 43, 88), for the reasons set forth on August 27, 2007.

The November 7, 2007 gives conflicting signals as to the result of this request. On the one hand, office action page 2, second full paragraph appears to have agreed, upon reconsideration, to rejoin groups VII and IX

Upon reconsideration of the restriction requirement and applicants' request and traversal, groups VII (43, 88, 90) and IX (43-44, 88) would be rejoin with the elected invention, group VIII (claims 43 and 88).

Consistent with this, the Examiner has considered claim 44 (group IX) and indeed indicated that it would be allowable if rewritten in independent form (OA p. 11, last double spaced paragraph). And the Examiner has also considered claim 90, rejecting it on written description (OA p. 4, last para.) and indefiniteness (OA p. 5, second-to-last para.) grounds.

On the other hand, the continuation page of the office action summary lists claim 90 (group VII) as withdrawn from consideration.

Clarification is requested. In the meantime, since claims 44 and 90 were clearly examined, we have treated them as considered for purposes of the claim listing.

1.2. In response to the species restriction, applicants elected the compound HY6, but requested that the species restriction be withdrawn on the ground that a generic claim is allowable.

The Examiner says that this cannot yet be done because "the claimed generic compound has not been found allowable".

The only claim rejected over prior art is claim 88 (OA pp. 7-11). Claim 43, which the restriction (page 5, last

line) concedes to be generic, was rejected only on written description and indefiniteness grounds, which we believe to have been overcome. In addition, if claim 43 is generic, so too is new claim 91, against which the indefiniteness rejection is clearly irrelevant.

In view of the arguments presented below concerning written description and indefiniteness, claim 43 should be allowed, and the species restriction withdrawn.

1.3. The examiner has indicated that the isolated ligand HY6 of claim 44 is allowable. It follows that a claim to an isolated ligand-protein binding pair (combination) in which the ligand (subcombination) is HY6 should be allowable, cp. new claims 93 and 94.

PCT Administrative Instructions Annex B, para. (c) (i) says "no problem arises in the case of a combination/subcombination situation where the subcombination claim avoids the prior art and the combination claim includes all features of the subcombination".

If generic claim 43 is held to be allowable, then claim 46 should be rejoined, and new claims 95 and 96 should be considered.

1.4. Under MPEP 821.04, if applicants have an allowable product claim, they are entitled to consideration of a dependent method-of-use claims (or method-of-use claims which otherwise include all limitations of that product claim). The PTO has applied this principle even in national stage cases.

New method claim 99 is directed to use of HY6 (cp. Claim 44) in binding a protein, the latter being further specified in claim 100.

Claim 99 is dependent on new method claims 97 and 98, whose consideration is appropriate if claim 43 is deemed allowable.

2. Amended claims

Claim 43 has been rewritten as an independent claim, i.e. no longer dependent on claim 88, and further amended by specifying R1 as a side chain of "an amino acid selected from the group consisting of amino acids mentioned in tables 1, 2, 3, 7 and 9". Support for this amendment can be found in the description at page 39, lines 22-23.

Claim 43 no longer requires (by virtue of dependency on 88) identification of the ligand by the process of claim 3. However, such process limitation appears in new method claim 101.

Claim 46 has been amended to depend on claim 95, instead of claim 88, and added the phrase "comprising a ligand and a protein".

Claim 88 has been cancelled.

Claim 89 has been amended to depend on claim 43, instead of claim 88.

Claim 91 is a new independent claim having support in the description at page 39, lines 15-30.

Claim 92 is a new dependent claim, dependent on new claim 90, specifying preferred embodiments of R1, R2 and R3; these preferred embodiments have support in the description at page 39, lines 23-33.

New claims 93-101 have already been discussed in section 1.

3. Specification (OA page 4)

3.1. In response to the objection to the abstract, a replacement abstract, beginning on a separate sheet, is enclosed. Kindly file the enclosed abstract on a separate sheet, in response to the objection to lack of same.

3.2. With regard to **claim 43**, the Examiner states that there is no antecedent basis in the specification for the text "dotted lines indicates an optional carbonyl", and examiner

further speculates that the drawn dotted line shows stereochemistry.

First, we have solved the problem of antecedent basis by amending the specification at page 39 to recite "In formula IV above, the double dotted line represents an optional carbonyl bond."

The underlying issue, which is whether such insertion would violate the new matter prohibition (in the specification) or the written description requirement (for the corresponding claim), is discussed below.

First, it is a common practice to use a dotted line for indication of an optional bond.

In the international patent classification, A01N, the note (11) in the section titled "Biocides" states, "In groups A01N 25/00 to A01N 65/00, ... [a] dotted line between atoms indicates an optional bond, e.g., indicates one or two single bonds or a double bond." (Exhibit A)

Numerous US patents follow this convention. A search on the USPTO database, for patents issued since 1976, revealed 263 hits for the query "("dotted line" AND "optional bond")" (Exhibit B). We recognize that this query doesn't guarantee that the two terms appear in the same sentence. However, we inspected the five earliest patents in the search results and they all clearly followed the "dotted line is an optional bond" convention:

Van der Burg, USP 3,950,425 (1976)

Amino-substituted tetracyclic compounds

Abstract: "The dotted line means an optional C-C bond"

Pfeiffer, USP 3,953,422 (1976)

Deoxyglucose derivatives

Claim 8, "the dotted line is an optional carbon-carbon bond"

DeFranco, USP 3,975,399 (1976)

1,5-Disubstituted-2-pyrrolidinones, -3-pyrrolin-2-ones, and -4-pyrrolin-2-ones

Statement of the Invention, after the first formula

"a, b and c (the dotted lines) are optional additional bonds
...."

Sasajima, USP 3,979,390 (1976)

Butyrophenone derivatives and production thereof

Claim 1

the dotted line is an optional bond

Rovynak, USP 4,002,749

Substituted indolinones

Claim 1

"the dotted line represents an optional bond"

Nor is this an old practice which has fallen into disrepute. The most recent patent on Exhibit B, Zaveri, USP 7,329,687, Flavanoid compounds as chemotherapeutic, chemopreventive, and antiangiogenic agents, states "the phrase an "optionally present" bond as indicated by a **dotted line** in the chemical formulae herein means that a bond may or may not be present."

Nor would the search strategy of Exhibit B capture all relevant patents. For example, it would not find the statement "The bond represented by the dotted line in Figure _ is optional" since that wouldn't meet the "optional bond" criterion. We also know that there are also US patents which state that "the **dashed** line" is an optional bond, see e.g. 7,176,215 and 7,268,119.

Secondly, while a dotted line can represent a bond connecting to a group below the plane of the paper, applicants

clearly use a "broken wedge" for that purpose. See e.g. compounds 3, 5, 8-19, 26, 27, 30-32, 39-43, 46-52, 69, 70, 75.

This contrasts better with the use of a solid wedge to show a bond connecting to a group above the plane of the paper, as in compounds 20, 21, 25 etc. See particularly compound 26 which features both the broken wedge and the solid wedge.

The 1996 IUPAC recommendations (Ex. C) suggested the use of a combination of the bold (solid black) wedge to show a group above the plane of the drawing (wedge tapering toward the plane), and of a broken bar (bar composed of short parallel lines) to show a group below the plane. It recommended against use of either dotted lines (the examiner's interpretation) or the broken wedge (used by applicant) to show stereochemistry.

It is clear from context that with respect to formula IV, the dotted lines cannot represent stereochemistry, as the skilled person will know that a carbonyl group cannot give rise to a stereogenic center at a carbon atom (i.e., two single bonds and one double bonded oxygen, instead of four single bonds).

Finally, the specification, at page 39, lines 28-29, explicitly identifies the carbonyl group as an optional group.

Making explicit was clearly implicit, i.e., that the dotted line represents an optional bond, is not addition of new matter and hence there is no violation of the written description requirement.

However, as the exact phrase used in claim 43 was not explicitly set forth in the original specification, we have included a new independent claim (91) and a new dependent claim (92), from which the questioned phrase is omitted, and the wording of the relevant features is word by word as found in the description at page 39, lines 15-33.

4. Written Description/New Matter Rejection (OA pp. 4-5)

4.1. The Examiner rejects **claims 43 and 90** as containing subject matter which was not described in the specification in such a way as to convey that the inventors was in possession of the invention at the time of filing.

The Examiner suggests that because claim 43 recites a generic formula for the ligand, it appears inconsistent with base claim 88, which requires that the ligand have been identified as binding a protein target by the method of claim 3. The Examiner further suggests that claim 43 recites a ligand library, rather than an identified ligand.

Claim 43 has been amended to refer per se to the ligands of formula IV (basis at P39, L15-19) without regard to whether they have been identified by the method of claim 3. Hence, the alleged inconsistency has been eliminated.

We assume that claim 90 was rejected solely by virtue of its dependency on claim 43, since it was not separately argued.

4.2. The Examiner did not appear to explicitly reject claim 43 for lack of written description on the basis of the "dotted line" issue discussed above. However, to the extent that such rejection was intended, it is traversed for the reasons already explained.

5. Indefiniteness rejections (OA pp. 5-6)

5.1. As **claim 88** is cancelled we respectfully submit that the objection with regard to claim 88, is now obsolete.

5.2. Regardless of whether the phrase "dotted lines indicates an optional carbonyl" lacks antecedent basis or has new matter/written description problems (which it doesn't, see section 3.2 above), the Examiner has not explained how this phrase is in any way vague or ambiguous. It is clearly definite in meaning.

5.3. The issue raised in the point misnumbered "4" on page 6 of the action, relates to the use of the term "unnatural amino acids" in connection with R1, in claim 43. Claim 43 has now been amended by specifying the side chains as side chains of "an amino acid selected from the group consisting of amino acids mentioned in tables 1, 2, 3, 7 and 9". Support for this amendment can be found at page 39, lines 22-23.

5.4. It is stated by the Examiner, in the point misnumbered "5" on page 6 of the action, that **claim 90** is indefinite due to the reference to tables comprising side chains that are preferred embodiments of residues of formula IV. The Examiner argues, citing MPEP 2173.05(s), that incorporation by reference to specific tables "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a figure or a table into the claim".

We believe that the "exceptional circumstances" contemplated by MPEP 2173.05(s), whereby reference to tables is permissible, apply here.

Claim 90 (as well as amended claim 43) cites tables 1, 2, 3, 7 and 9. Compounds 1-20 appear in Table 1, 21-38 appear in Table 2, 39-52 in Table 3, 54, 55a, 55b, and 56-81 in Table 7, and 103-128 in Table 128. The structure of each of these 108 compounds is shown graphically. For some compounds (1, 3-35, 39-54, 63), there is also an abbreviation (which might or might not be an abbreviation standard in the art), but for the others there is only the structure.

Hence, if we simply copied tables 1, 2, 3, 7 and 9 into claims 90 and 43, it would not be "defining the invention in words". To define it in words, we would have to convert all 108 structural formulae into the corresponding systematic chemical name (or equivalent semi-systematic or trivial name).

It would be easy for applicants to make inadvertent errors in this process, and the examiner would need to check each of the 108 names against the formulae to enforce the prohibition against new matter.

It is also clearly "more concise" to simply reference tables 1, 2, 3, 7 and 9, rather than to repeat them twice in the claims.

Claims Rejections - 35 USC § 102 , and Claims Rejections - 35 USC § 103

As **claim 88** is cancelled we respectfully submit that the objection with regard to claim 88, is now moot.

Claim 44 was objected to as being dependent upon a rejected base claim; said claim has now been rewritten as an independent claim¹. Accordingly, we respectfully submit that claim 44 is now allowable.

None of the other examined claims were rejected over prior art and thus, since they were also amended to eliminate dependency on claim 88, they should be allowable over the prior art.

Respectfully submitted,
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¹ It does not incorporate the process limitations of claim 3 but those are irrelevant to patentability as explained